Contents lists available at ScienceDirect

# **Obesity Pillars**

journal homepage: www.journals.elsevier.com/obesity-pillars

# Prevalence of cardiovascular events among transgender adults with obesity: A population-based analysis

Adhvithi Pingili<sup>a,\*</sup>, Roopeessh Vempati<sup>b</sup>, Madhusha Vemula<sup>c</sup>, Mohit Lakkimsetti<sup>d</sup>, Hasmitha Madhavaram<sup>e</sup>, Athmananda Nanjundappa<sup>f</sup>, Jyotsna Gummadi<sup>f</sup>, Sandeep Singh<sup>g</sup>, Rupak Desai<sup>h</sup>, Praveena Sunkara<sup>i</sup>

<sup>a</sup> Department of Internal Medicine, MedStar Union Memorial Hospital, Baltimore, MD, USA

<sup>b</sup> Department of Internal Medicine, Trinity Health Oakland Hospital, Pontiac, MI, USA

<sup>c</sup> Department of General Medicine, Malla Reddy Institute of Medical Sciences, Hyderabad, Telangana, India

<sup>d</sup> Department of General Medicine, Mamata Medical College, Khammam, Telangana, India

<sup>e</sup> Department of Internal Medicine, Morristown Medical Centre, Morristown, NJ, USA

<sup>f</sup> Department of Medicine, MedStar Franklin Square Medical Centre, Baltimore, MD, USA

<sup>g</sup> University Hospitals of North Midlands MHS Trust, Stroke-on-Trent, UK

<sup>h</sup> Independent Researcher, Outcomes Research, Atlanta, GA, USA

<sup>i</sup> Department of Internal Medicine, Passion Health Primary Care, Denton, TX, USA

## ARTICLE INFO

## ABSTRACT

The poster was presented at the AHA23 meeting.

Keywords: Transgender Gender-affirming care Obesity Cardiovascular risk factors Major adverse cardiac and cerebrovascular events

## cisgender population, little is known about its impact on CV events in transgender individuals. Our study aimed to establish the prevalence of obesity and CV events in transgender adults. *Methods*: We conducted a retrospective cohort comparative study utilizing the U.S. National Inpatient Sample

Introduction: Although obesity and its impact on cardiovascular (CV) events have been extensively studied in the

2020 database. We identified admissions of transgender patients with administrative codes. Later, these patients were divided into obesity and non-obesity cohorts. Multivariable regression analysis was then performed for inhospital all-cause mortality, acute myocardial infarction, acute ischemic stroke, cardiac arrest, pulmonary embolism and, major adverse cardiovascular and cerebrovascular events (MACCE).

*Results*: In 2020, 19,345 transgender patients were admitted; 16,390 (84.7 %) had no obesity, and 2,955 (15.3 %) had obesity. The median age was 31 years in the non-obesity cohort and 37 years in the obesity cohort. Transgender men comprised 54.5 % of the non-obesity cohort and 47.9 % of the obesity cohort. Common baseline conditions in the non-obesity and obesity cohorts, respectively, included hypertension (20.7 % vs. 43.5 %), diabetes (10.2 % vs. 32.5 %), chronic pulmonary disease (18.9 % vs. 27.7 %), and hyperlipidemia (11.5 % vs. 25 %). MACCE was observed in 2.3 % of the non-obesity cohort compared to 5.4 % in the obesity cohort. A statistically significant association was found in MACCE [odds ratio (OR) 2.1, 95 % confidence interval (CI) 1.24–3.55, p = 0.006] and cardiac arrest [OR 3.92, 95 % CI 1.11–12.63, p = 0.022] among transgender patients with obesity. *Conclusion:* We observed increased odds of MACCE and cardiac arrest in transgender patients with obesity, possibly due to obesity and CV risk factors like hypertension, diabetes, and hyperlipidemia. Further large-scale comparative studies are needed to better understand obesity's impact on CV outcomes in the transgender population.

\* Corresponding author.

https://doi.org/10.1016/j.obpill.2024.100125

Received 4 July 2024; Received in revised form 11 August 2024; Accepted 12 August 2024

Available online 13 August 2024





*E-mail addresses*: adhvithi.pingili@medstar.net (A. Pingili), roopeshgupta6666666@gmail.com (R. Vempati), madhushavemula@gmail.com (M. Vemula), mlakkimsetti@gmail.com (M. Lakkimsetti), hasmitha.john@gmail.com (H. Madhavaram), athmanand@gmail.com (A. Nanjundappa), jyotsnagummadil1@gmail.com (J. Gummadi), sandeepkcsingh@gmail.com (S. Singh), drrupakdesai@gmail.com (R. Desai), praveenasunkara@gmail.com (P. Sunkara).

<sup>2667-3681/© 2024</sup> The Author(s). Published by Elsevier Inc. on behalf of Obesity Medicine Association. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

## 1. Introduction

In recent years, understanding the health-related disparities associated with transgender care has gained increased recognition. The term "transgender" encompasses individuals whose gender identities and expressions may differ from the sex they were assigned at birth [1]. Transgender people may undergo medical interventions such as hormone therapy or gender-affirming surgery to align their physical characteristics with their gender identity [1]. The estimated prevalence of transgender individuals in the USA is approximately 0.5 % [2,3]. Given that the prevalence of transgender population has been growing due to increased visibility, acceptance, and understanding within the general population, one area that warrants particular attention is the prevalence and impact of obesity in this population. Obesity and its impact on cardiovascular (CV) complications have been extensively studied in the cisgender population. However, there is a notable gap in understanding its implications for CV health within transgender communities. This focus is underscored by the significant rise in obesity prevalence globally, nearly tripling between 1975 and 2016, as per the World Health Organization (WHO) [4]. Through this study, we sought to establish the prevalence of obesity and its impact on CV events in the transgender population.

#### 2. Methods

## 2.1. Source of the study

We conducted a retrospective cohort comparative study utilizing the United States (US) National Inpatient Sample (NIS) 2020 database. NIS is a part of the Healthcare Cost and Utilization Project (HCUP) and is the most extensive US all-payer inpatient healthcare dataset that is available to the public. It includes information on the discharge of 20 % of hospitals from over 47 states. On average, there are 7 million discharges yearly, which amounts to more than 35 million discharges nationwide. Each NIS inpatient admission contains a primary diagnosis and up to 39 secondary discharge diagnoses. As the NIS has de-identified data, our study did not require Institutional Review Board (IRB) approval. For more information about the database, please visit the HCUP website [https://hcup-us.ahrq.gov/nisoverview.jsp].

## 2.2. Study population

In the NIS database, we identified transgender adults using F64.x (gender identity disorders) or Z87.890 (personal history of sex reassignment surgery) International Classification of Diseases, 10th Revision, Clinical Modification codes (ICD-10-CM). We formed two groups, one composed of transgender adults without obesity and the other group of transgender adults with obesity. We assessed baseline characteristics like age, sex, race, median household income, payer; baseline medical conditions such as hypertension, diabetes mellitus, hyperlipidemia, prior myocardial infarction (MI), prior stroke/transient ischemic attack (TIA), prior venous thromboembolism, peripheral vascular disease, tobacco use disorder, alcohol abuse, drug abuse, cocaine abuse, cannabis use disorder, cancer, chronic kidney disease, depression, acquired immune deficiency syndrome (AIDS), chronic pulmonary disease, and; hospital-level characteristics such as an elective/non-elective admission, region, location, and teaching status.

#### 2.3. Study findings

Along with assessing the prevalence of obesity, the primary aim of the study was to evaluate the prevalence of in-hospital CV events in transgender adult patients with and without obesity. The CV events examined included all-cause mortality, acute myocardial infarction (AMI), cardiac arrest, acute ischemic stroke (AIS), pulmonary embolism (PE), and major adverse cardiovascular and cerebrovascular events (MACCE), which is a composite of all-cause mortality, AMI, cardiac arrest, and AIS. The study also compared the two groups' discharge disposition, length of stay, and hospital costs.

#### 2.4. Statistical analysis

We applied the discharge weight provided in the database to generate the national estimates. Pearson Chi-square test for categorical variables and Mann Whitney U for continuous variables were used to compare the baseline demographics and hospital characteristics between the groups (with or without obesity) among transgender adult hospitalizations. The categorical and continuous variables were expressed in percentages and mean  $\pm$  SD, respectively. A two-tailed p-value of <0.05 was used to decide the statistical significance.

After regulating for age, sex, race, median household income, payer type, length of stay, hospitalization cost, hospital location, teaching status, hospital region, and all baseline medical conditions, a multivariable regression model assessed the risk of all-cause mortality, AMI, cardiac arrest, AIS, PE, and MACCE. We evaluated predictors of MACCE by univariate analysis, and then clinically relevant variables were integrated into the multivariable analysis. Adjusted odds ratio (OR), 95 % confidence interval (CI), and p-values were considered to account for logistic regression results. We utilized IBM SPSS Statistics 25.0 (IBM Corp, Armonk, New York) software for all the statistical analyses.

#### 3. Results

#### 3.1. Patient-level demographics

According to the 2020 NIS, 19,345 transgender patients were admitted to hospitals. Of those admitted, 16,390 (84.7 %) did not have obesity, while 2,955 (15.3 %) had obesity. The median age of patients in transgender adults without obesity is 31 years vs. 37 years in those with obesity. Among transgender adults without obesity, 54.5 % were transgender men, and 45.5 % were transgender women, whereas among transgender adults with obesity, 47.9% were transgender men, and 52.1 % were transgender women. There were 66.6 % Whites, 18.3 % Blacks, and 11.6 % Hispanics in the non-obesity cohort vs. 66.5 % Whites, 18.8 % Blacks, and 11.7 % Hispanics. For income groups, 29.6 % of both the non-obesity and obesity cohorts were in the lower household income bracket. 25.3 % of the non-obesity cohort compared to 27.9 % of the obesity cohort represented the lower-middle income group. The middleincome group had 23.2 % of the non-obesity cohort versus 25.5 % of the obesity cohort. Finally, 21.9 % of the non-obesity cohort was in the upper income group, whereas only 17.0 % of the obesity cohort fell into this category [Table 1].

## 3.2. Hospital-level demographics

19.2 % of transgender adults without obesity had Medicare, vs. 27.5 % of transgender adults with obesity had Medicare compared to Medicaid (39.2 % vs. 44 %), private insurance (35 % vs. 32.6 %), and self-pay (6.3 % vs. 5.8 %). Non-elective admissions were less frequent in transgender adults without obesity compared to transgender adults with obesity (77.8 % vs. 81.6 %). Overall, most of the transgender patients without and with obesity were admitted to urban-teaching hospitals (84 % vs. 79.2 %), then into urban non-teaching hospitals (11.4 % vs. 15.4 %), and lastly, in the rural setting (4.7 % vs. 5.4 %). Admissions were almost equally distributed across regions for transgender adults without and with obesity: West (27.4 % vs. 28.3 %), Midwest (23.1 % vs. 27.1 %), South (24.9 % vs. 23.5 %), Northeast (24.6 % vs. 21.2 %) [Table 1].

## 3.3. Baseline medical conditions

Overall, statistically prevalent baseline medical conditions among transgender patients without and with obesity were as follows:

#### Table 1

Baseline characteristics of hospitalized transgender adult patients, 2020.

Characteristics of Transgender adult patients		Without Obesity 16,390 (84.7 %)	With Obesity 2,955 (15.3 %)	Total 19,345 (100 %)	p-value
Age in years at admission	Median	31	37	32	< 0.001
	18–44	12350 (75.4 %)	1905 (64.5 %)	14255 (73.7 %)	
	45–64	2905 (17.7 %)	795 (26.9 %)	3700 (19.1 %)	
	>/ = 65	1135 (6.9 %)	255 (8.6 %)	1390 (7.2 %)	
Gender	Man	8375 (54.5 %)	1360 (47.9 %)	9735 (53.4 %)	< 0.001
	Woman	7000 (45.5 %)	1480 (52.1 %)	8480 (46.6 %)	
Race	White	10030 (66.6 %)	1785 (66.5 %)	11815 (66.6 %)	< 0.001
	Black	2760 (18.3 %)	505 (18.8 %)	3265 (18.4 %)	
	Hispanic	1740 (11.6 %)	315 (11.7 %)	2055 (11.6 %)	
	Asian/PI	395 (2.6 %)	40 (1.5 %)	435 (2.5 %)	
	Native Americans	130 (0.9 %)	40 (1.5 %)	170 (1.0 %)	
Median household income national quartile for	0-25 (lower)	4525 (29.6 %)	810 (29.6 %)	5335 (29.6 %)	< 0.001
patient ZIP code	26-50 (lower-middle)	3875 (25.3 %)	765 (27.9 %)	4640 (25.7 %)	
	51-75 (middle)	3555 (23.2 %)	700 (25.5 %)	4255 (23.6 %)	
_	76-100 (upper)	3350 (21.9 %)	465 (17.0 %)	3815 (21.1 %)	
Payer type	Medicare	3010 (19.2 %)	785 (27.5%)	3/95 (20.4 %)	< 0.001
	Medicaid	6165 (39.2 %)	970 (34.0 %)	7135 (38.4 %)	
	Private	5495 (35%)	930 (32.6 %)	6425 (34.6 %)	
	Self-pay	985 (6.3 %)	165 (5.8 %)	1150 (6.2 %)	
The effect	No charge	55 (0.4 %)	-	60 (0.3 %)	-0.001
Elective	Non-elective	12/35 (77.8 %)	2410 (81.6 %)	15145 (88.4 %)	<0.001
Heavitel leastion and teaching status	Elective	3625 (22.2 %)	545 (18.4 %)	41/0 (21.6 %)	<0.001
Hospital location and teaching status	Rufai Urban non taashing	703 (4.7 %) 1865 (11 4 %)	100 (5.4 %) 4EE (1E 4.04)	925 (4.8 %)	< 0.001
	Urban tooching	1805 (11.4 %)	455 (15.4 %)	2520 (12.0 %)	
Hospital region	Northoast	13700 (84.0 %)	2340 (79.2 %)	10100 (83.2 %) 46E (24.1.04)	<0.001
Hospital legion	Midwort	4040 (24.0 %)	800 (27.1.04)	403 (24.1 %)	<0.001
	South	4080 (24.9.%)	605 (22.5 %)	4380 (23.7 %)	
	West	4490 (27.4 %)	835 (28.3 %)	5325 (27.5 %)	
Baseline medical conditions	West	490 (27.4 70)	000 (20.0 70)	3323 (27.370)	
Hypertension		3390 (20.7 %)	1285 (43.5 %)	4675 (24.2 %)	< 0.001
Diabetes Mellitus		1675 (10.2 %)	960 (32.5 %)	2635 (13.6 %)	< 0.001
Hyperlipidemia		1880 (11.5 %)	740 (25.0 %)	2620 (13.5 %)	< 0.001
Prior MI		335 (2.0 %)	105 (3.6 %)	440 (2.3 %)	< 0.001
Prior stroke/TIA		370 (2.3 %)	85 (2.9 %)	455 (2.4 %)	00.041
Prior venous thrombo-embolism		545 (3.3 %)	185 (6.3 %)	730 (3.8 %)	< 0.001
Peripheral vascular disease		265 (1.6 %)	40 (1.4 %)	305 (1.6 %)	00.290
Tobacco use disorder		3415 (20.8 %)	610 (20.6 %)	4025 (20.8 %)	00.812
Alcohol abuse		1365 (8.3 %)	200 (6.8 %)	1565 (8.1 %)	00.004
Drug abuse		2935 (17.9 %)	360 (12.2 %)	3295 (17.0 %)	< 0.001
Cocaine abuse		740 (4.5 %)	55 (1.9 %)	795 (4.1 %)	< 0.001
Cannabis use disorder		2570 (15.7 %)	325 (11.0 %)	2895 (15.0 %)	< 0.001
Cancer		485 (3.0 %)	110 (3.7 %)	595 (3.1 %)	00.027
Chronic kidney disease		930 (5.7 %)	360 (12.2 %)	1290 (6.7 %)	< 0.001
AIDS		1725 (10.5 %)	190 (6.4 %)	1915 (9.9 %)	< 0.001
Depression		3310 (20.2 %)	770 (26.1 %)	4080 (21.1 %)	< 0.001
Chronic pulmonary disease		3100 (18.9 %)	820 (27.7 %)	3920 (20.3 %)	< 0.001
Hypothyroidism		935 (5.7 %)	370 (12.5 %)	1305 (6.7 %)	< 0.001
Cardiovascular events					
All-cause mortality		95 (0.6%)	45 (1.5 %)	140 (0.7 %)	< 0.001
Cardiac arrest		35 (0.2 %)	35 (1.2 %)	70 (0.4 %)	< 0.001
AMI		175 (1.1 %)	75 (2.5%)	250 (1.3 %)	< 0.001
AIS		100 (0.6%)	25 (0.8%)	125 (0.6 %)	< 0.001
MACCE		375 (2.3 %)	160 (5.4 %)	535 (2.8 %)	< 0.001
Disposition of the Patient	Routine	13135 (80.6 %)	2175 (74.7 %)	15310 (79.7 %)	< 0.001
	Transfer to a short-term hospital	215 (1.3 %)	60 (2.1 %)	275 (1.4 %)	
	Transfer other: SNF, ICF	1320 (8.1 %)	305 (10.5 %)	1625 (8.5 %)	
	Home health care	955 (5.9 %)	325 (11.2 %)	1280 (6.7 %)	
	Against medical advice	665 (4.1 %)	45 (1.5 %)	710 (3.7 %)	
Length of the stay (days), Median (IQR)		4	4	4	< 0.001
Adjusted cost (USD), Median (IQR)		33670	37360	34083	< 0.001

TIA: transient ischemic attack, VTE: venous thromboembolism, AIDS: acquired immunodeficiency syndrome, PI: pacific islander, MACCE: major adverse cardiovascular and cerebrovascular events, AMI: acute myocardial infarction, AIS: acute ischemic stroke, SNF: skilled nursing facility, ICF: intermediate care facility; USD: United States dollar

"Sex" is referred as biologic female or male where as "gender" is referred to self-identification, socially constructed attitudes, roles, feelings, behaviors and personal experience that may not aligned with the sex recorded at birth.

Obesity is defined as body mass index of 30 kg/m<sup>2</sup> or greater.

All the other variables are based on administrative reporting in the National Inpatient Sample Database.

#### A. Pingili et al.

Table 2

Multivariable logistic regression odds of cardiovascular events among hospitalized transgender adults with obesity.

Cardiovascular events among hospitalized transgender adults with obesity	Odds ratio	Lower limit of CI	Upper limit of CI	P- Value
MACCE	2.10	1.24	3.55	0.006
All-cause mortality	2.09	0.81	5.36	0.127
AMI	1.82	0.85	3.93	0.125
Cardiac arrest	3.92	1.22	12.63	0.0220
AIS	1.34	0.39	4.62	0.638
Pulmonary embolism	2.18	0.83	5.72	0.113

Multivariable regression models were adjusted for age, gender, race, income quartile, payer type, hypertension, diabetes, hyperlipidemia, peripheral vascular disease, tobacco use disorder, prior MI, prior TIA/stroke, prior VTE, cancer, chronic kidney disease, AIDS, alcohol abuse, drug abuse, depression.

TIA: transient ischemic attack, VTE: venous thromboembolism, AIDS: acquired immunodeficiency syndrome, MACCE: major adverse cardiovascular and cerebrovascular events, AMI: acute myocardial infarction, AIS: acute ischemic stroke.

hypertension (20.7 % vs. 43.5 %), diabetes mellitus (10.2 % vs. 32.5 %), hyperlipidemia (11.5 % vs. 25 %), prior MI (2 % vs. 3.6 %), prior stroke/ TIA (2.3% vs. 2.9 %), prior venous thromboembolism (3.3 % vs. 6.3 %), alcohol abuse (8.3 % vs. 6.8 %), drug abuse (17.9 % vs. 12.2 %), cocaine abuse (4.5 % vs.1.9 %), cannabis use disorder (15.7 % vs.11 %), cancer (3 % vs. 3.7 %), chronic kidney disease (5.7 % vs. 12.2 %), %), AIDS (10.5 % vs 6.4 %), depression (20.1 % vs. 26.1 %), chronic pulmonary disease (18.9 % vs. 27.7 %), and hypothyroidism (5.7 % vs. 12.5 %). The non-statistically significant health conditions among transgender patients without and with obesity are peripheral vascular disease (1.6 % vs.1.4 %) and tobacco use disorder (20.8 % vs. 20.6 %).

#### 3.4. Prevalence of MACCE

In hospitalized transgender adults, the prevalence of MACCE was 2.3 % among those without obesity, while it was 5.4 % among the patients with obesity. All-cause mortality among hospitalized transgender adult patients without obesity was 0.6 %, while it was 1.5 % among those with obesity. 1.1 % of those without obesity had AMI, and 2.5 % of those with obesity had AMI. 0.2 % of the non-obesity cohort and 1.2 % of the obesity cohort had a cardiac arrest. Among the non-obesity cohort, 0.6 % had AIS, while 0.8 % of the obesity cohort had AIS [Table 1]. A statistically significant association was observed on multivariable logistic regression for MACCE [OR: 2.1, 95 % confidence interval (CI) 1.24-3.55, p = 0.006] and cardiac arrest (OR: 3.92, 95 % CI: 1.11–12.63, p = 0.022) among the obesity cohort of the transgender population, with age being the important predictor of MACCE (OR: 1.04, 95 % CI: 1.01–1.07, P = 0.023). Surprisingly, no statistically significant association was observed with in-hospital all-cause mortality (OR: 2.09, 95 % CI: 0.81–5.36, p = 0.127), AMI (OR: 1.82, 95 % CI: 0.85–3.93, p = 0.125), AIS (OR: 1.34, 95 % CI: 0.39-4.62, p = 0.638) and PE (OR: 2.18, 95 % CI: 0.83–5.72, p = 0.113) [Table 2].

#### 3.5. Discharge destination, hospital duration, and financial impact

Most of the patients from both non-obesity and obesity cohorts were discharged routinely (80.6 % vs. 74.7 %), followed by transfer to other centers like skilled nursing facilities, intermediate care facilities, etc. (8.1 % vs.10.5 %), home health care (5.9% vs. 11.2 %), against medical advice (4.1 %. vs. 1.5 %), transfer to a short-term hospital (1.3 % vs. 2.1 %). The median length of the hospital stay among non-obesity and obesity patients was four days, while it was three days among non-MHO patients. The median hospital costs among the non-obesity cohort were 33,670 USD, while it was 37,360 USD among the obesity cohort [Table 1].

## 4. Discussion

In this real-world analysis regarding prevalence and impact of obesity in the transgender population, we found several key findings: 1) the prevalence of obesity among the transgender population is 15.3 %

among inpatient admissions; 2) we found that transgender populations with obesity are at increased odds of MACCE by at least two times and cardiac arrest by at least four times when compared to transgender patients without obesity; 3) in addition, we also found that age is an important predictor of MACCE among transgender patients with obesity. To the best of our knowledge, there are no previous studies that discussed the impact of obesity on CV events in the transgender population.

According to a study by Brown et al. in veterans, transgender patients are at increased odds of obesity by 1.58 times when compared to cisgender patients [5]. In another study by Dragon et al. in veterans, the prevalence of obesity is 31.3 % among transgender adults compared to 17.2 % among cisgender peers [6]. In our study, the prevalence of obesity among transgender adults admitted to hospitals is 15.3 %. The higher prevalence of obesity among transgender patients noted in the previous studies is likely multifactorial. Firstly, gender-affirming hormone treatment causes an increase in body weight; while testosterone increases muscle mass, estrogens, together with antiandrogens, increase fat mass, as per existing literature [7,8]. Second, when it comes to eating habits and exercise, as per one study, transgender adults have eating disorders, including binging, when compared to their cisgender peers, and per one study, transgender youth are less likely to exercise, which could be the reason why obesity is more prevalent in transgender adults [9,10]. Third, the increased burden of mental health disorders and gender minority stress keeps transgender adults away from engaging in healthful behaviors such as accessing insurance and healthcare, including medications like glucagon-like peptide-1 receptor agonists when compared to cisgender, which can increase the prevalence of obesity [11-13].

As with the cisgender population, we observed that obesity increases MACCE and cardiac arrest in transgender patients as well [14,15]. This association can be attributed to multiple factors. According to existing literature, obesity is a well-established risk factor for CV events, both directly and indirectly [14,15]. Obesity directly contributes to CV events by increasing systemic and vascular inflammation, which leads to endothelial dysfunction and the development of atherosclerotic lesions [16,17]. Indirectly, obesity promotes the development of CV risk factors such as hypertension, diabetes mellitus, and hyperlipidemia, all of which are known to elevate the risk of MACCE and cardiac arrest [14,15, 18,19] In our study, these risk factors were significantly more prevalent among patients with obesity compared to those without, underscoring the link between obesity-increased CV risk factors and events in transgender patients. Moreover, transgender adults face a higher burden of mental health disorders, and obesity can exacerbate psychological stress, depression, and anxiety. These mental health conditions can affect treatment adherence and lifestyle modifications, potentially causing CV events [11-13,20-22]. Similar to existing evidence, we found that depression was more prevalent among transgender patients with obesity, which could be one of the reasons why CV events are more prevalent in this group compared to those without obesity. Other medical conditions like chronic pulmonary disease and hypothyroidism, which are associated with severe CV events, are highly prevalent in

transgender patients with obesity in our study [23,24]. Additionally, individuals with obesity may experience reduced physical activity due to impaired mobility, which lowers energy expenditure and creates a vicious cycle of weight gain and escalating CV risk [25].

We also found that, like in cisgender adults with obesity, where age is an established nonmodifiable risk factor for CV events, we identified that age is an important predictor of MACCE events in transgender adults with obesity [26]. Nevertheless, it is noteworthy that, although our study found obesity to be associated with an increased risk of MACCE and cardiac arrest in the transgender population when compared to patients with no obesity, no significant association was observed between obesity and in-hospital all-cause mortality, AMI, AIS, or PE. These findings contrast with previous studies on obesity, which, although not differentiated between cisgender and transgender populations, revealed an increased risk for these CV events as well [14–17].

## 5. Limitations

Our study must be interpreted considering its limitations. Given the use of an inpatient registryin our study, findings are limited to inhospital events. Due to its retrospective nature, we were restricted to a homogeneous sample of hospitalized, mostly white patients, affecting our findings' generalizability. The retrospective design also limits our ability to establish causal relationships despite offering valuable insights into the intersection of obesity, transgender identity, and in-hospital CV events. Additionally, we could not explore how social determinants of health impact outcomes in this population. We could not establish mean body mass index (BMI) due to the unavailability of specific BMI categories. Moreover, as our study relied on ICD-10 codes to extract the study population, it may not fully capture the transgender population due to potential underreporting or over-reporting.

#### 6. Conclusion

In this large population study, we found an increased risk of MACCE and cardiac arrest among transgender patients with obesity when compared to those without obesity. This elevated risk may be attributed to obesity and other CV risk factors like hypertension, type 2 diabetes mellitus, and hyperlipidemia. However, no association was found between obesity and in-hospital mortality, AMI, AIS, and PE in transgender patients. Given the limited research focusing specifically on CV health in transgender adults with obesity, further studies are needed to clarify these findings and inform better care strategies for this population.

#### **Credit author Statement**

Conceptualization - Adhvithi Pingili; Resources – Adhvithi Pingili; Investigation – Adhvithi Pingili, Writing –original draft –; Adhvithi Pingili, Roopeessh Vempati, Madhusha Vemula, Mohit Lakkimsetti, Hasmitha Madhavaram; Writing – review and editing – Adhvithi Pingili, Athmananda Nanjundappa, Jyotsna Gummadi, Praveena Sunkara, Sandeep Singh, Rupak Desai; Validation – Praveena Sunkara; Supervision – Praveena Sunkara; Methodology – Rupak Desai; Formal Analysis – Rupak Desai; Software – Rupak Desai. All authors have read and agreed to the published version of the manuscript.

#### Funding source

None.

## Declaration

Artificial intelligence was not used during any stage of this manuscript.

#### Declaration of competing interest

None.

## References

- [1] Coleman E, Radix AE, Bouman WP, Brown GR, de Vries ALC, Deutsch MB, Ettner R, Fraser L, Goodman M, Green J, Hancock AB, Johnson TW, Karasic DH, Knudson GA, Leibowitz SF, Meyer-Bahlburg HFL, Monstrey SJ, Motmans J, Nahata L, Nieder TO, Arcelus J. Standards of care for the health of transgender and gender diverse people, version 8. International journal of transgender health 2022; 23(1):S1–259. https://doi.org/10.1080/26895269.2022.2100644.
- [2] Meerwijk EL, Sevelius JM. Transgender population size in the United States: a meta-regression of population-based probability samples. Am J Publ Health 2017; 107(2):e1–8. https://doi.org/10.2105/AJPH.2016.303578.
- [3] Downing JM, Przedworski JM. Health of transgender adults in the U.S., 2014-2016. Am J Prev Med 2018;55(3):336–44. https://doi.org/10.1016/j. amenre 2018 04 045
- [4] World Health Organization (WHO). Obesity and overweight fact sheet. https:// www.who.int/news-room/fact-sheets/detail/obesity-and-overweight. [Accessed 12 October 2021].
- [5] Brown GR, Jones KT. Mental health and medical health disparities in 5135 transgender veterans receiving healthcare in the veterans health administration: a case-control study. LGBT Health 2016;3(2):122–31. https://doi.org/10.1089/ lgbt.2015.0058.
- [6] Dragon CN, Guerino P, Ewald E, Laffan AM. Transgender Medicare beneficiaries and chronic conditions: exploring fee-for-service claims data. LGBT Health 2017;4 (6):404–11. https://doi.org/10.1089/lgbt.2016.0208.
- [7] Klaver M, Dekker MJHJ, de Mutsert R, Twisk JWR, den Heijer M. Cross-sex hormone therapy in transgender persons affects total body weight, body fat and lean body mass: a meta-analysis. Andrologia 2017;49(5). https://doi.org/10.1111/ and.12660. 10.1111/and.12660.
- [8] Kyinn M, Banks K, Leemaqz SY, Sarkodie E, Goldstein D, Irwig MS. Weight gain and obesity rates in transgender and gender-diverse adults before and during hormone therapy. Int J Obes 2021;45(12):2562–9. https://doi.org/10.1038/s41366-021-00935-x. 2005.
- [9] Nagata JM, Murray SB, Compte EJ, Pak EH, Schauer R, Flentje A, Capriotti MR, Lubensky ME, Lunn MR, Obedin-Maliver J. Community norms for the Eating Disorder Examination Questionnaire (EDE-Q) among transgender men and women. Eat Behav 2020;37:101381. https://doi.org/10.1016/j.eatbeh.2020.101381.
- [10] VanKim NA, Erickson DJ, Eisenberg ME, Lust K, Simon Rosser BR, Laska MN. Weight-related disparities for transgender college students. Health behavior and policy review 2014;1(2):161–71. https://doi.org/10.14485/HBPR.1.2.8.
- [11] Wanta JW, Niforatos JD, Durbak E, Viguera A, Altinay M. Mental health diagnoses among transgender patients in the clinical setting: an all-payer electronic health record study. Transgender health 2019;4(1):313–5. https://doi.org/10.1089/ trgh.2019.0029.
- [12] Christian R, Mellies AA, Bui AG, Lee R, Kattari L, Gray C. Measuring the health of an invisible population: lessons from the Colorado transgender health survey. J Gen Intern Med 2018;33(10):1654–60. https://doi.org/10.1007/s11606-018-4450-6.
- [13] Holt NR, Eldridge-Smith ED, Griffin JA, Stepleman LM, Drescher CF, Casanova T. Differences in health care access, utilization, and experiences among LGBTQ+ subgroups in the southern United States. Fam Community Health 2023;46(1): 58–68. https://doi.org/10.1097/FCH.0000000000340.
- [14] Powell-Wiley TM, Poirier P, Burke LE, Després JP, Gordon-Larsen P, Lavie CJ, Lear SA, Ndumele CE, Neeland IJ, Sanders P, St-Onge MP, American Heart Association Council on Lifestyle and Cardiometabolic Health; Council on Cardiovascular and Stroke Nursing; Council on Clinical Cardiology; Council on Epidemiology and Prevention; and Stroke Council. Obesity and cardiovascular disease: a scientific statement from the American heart association. Circulation 2021;143(21):e984–1010. https://doi.org/10.1161/CIR.0000000000000973.
- [15] Lopez-Jimenez F, Almahmeed W, Bays H, Cuevas A, Di Angelantonio E, le Roux CW, Sattar N, Sun MC, Wittert G, Pinto FJ, Wilding JPH. Obesity and cardiovascular disease: mechanistic insights and management strategies. A joint position paper by the World Heart Federation and World Obesity Federation. European journal of preventive cardiology 2022;29(17):2218–37. https://doi.org/ 10.1093/euripc/zwac187.
- [16] Ross R. Atherosclerosis is an inflammatory disease. Am Heart J 1999;138(5 Pt 2): S419-20. https://doi.org/10.1016/s0002-8703(99)70266-8.
- [17] Rocha VZ, Libby P. Obesity, inflammation, and atherosclerosis. Nat Rev Cardiol 2009;6(6):399–409. https://doi.org/10.1038/nrcardio.2009.55.
- [18] Fuchs FD, Whelton PK. High blood pressure and cardiovascular disease. Hypertension (Dallas, Tex. 2020;75(2):285–92. https://doi.org/10.1161/ HYPERTENSIONAHA.119.14240. 1979.
- [19] Miao B, Hernandez AV, Alberts MJ, Mangiafico N, Roman YM, Coleman CI. Incidence and predictors of major adverse cardiovascular events in patients with established atherosclerotic disease or multiple risk factors. J Am Heart Assoc 2020; 9(2):e014402. https://doi.org/10.1161/JAHA.119.014402.
- [20] Frasure-Smith N, Lespérance F. Depression and anxiety as predictors of 2-year cardiac events in patients with stable coronary artery disease. Arch Gen Psychiatr 2008;65(1):62–71. https://doi.org/10.1001/archgenpsychiatry.2007.4.
- [21] Tully PJ, Winefield HR, Baker RA, Denollet J, Pedersen SS, Wittert GA, Turnbull DA. Depression, anxiety and major adverse cardiovascular and

cerebrovascular events in patients following coronary artery bypass graft surgery: a five year longitudinal cohort study. Biopsychosoc Med 2015;9:14. https://doi.org/10.1186/s13030-015-0041-5.

- [22] Rajan TM, Menon V. Psychiatric disorders and obesity: a review of association studies. J Postgrad Med 2017;63(3):182–90. https://doi.org/10.4103/jpgm.JPGM\_ 712\_16.
- [23] Curkendall SM, Lanes S, de Luise C, Stang MR, Jones JK, She D, Goehring Jr E. Chronic obstructive pulmonary disease severity and cardiovascular outcomes. Eur J Epidemiol 2006;21(11):803–13. https://doi.org/10.1007/s10654-006-9066-1.
- [24] Zhang M, Sara JD, Matsuzawa Y, Gharib H, Bell MR, Gulati R, Lerman LO, Lerman A. Clinical outcomes of patients with hypothyroidism undergoing percutaneous coronary intervention. Eur Heart J 2016;37(26):2055–65. https:// doi.org/10.1093/eurheartj/ehv737.
- [25] Bays HE. Adiposopathy is "sick fat" a cardiovascular disease? J Am Coll Cardiol 2011;57(25):2461–73. https://doi.org/10.1016/j.jacc.2011.02.038.
- [26] Rodgers JL, Jones J, Bolleddu SI, Vanthenapalli S, Rodgers LE, Shah K, Karia K, Panguluri SK. Cardiovascular risks associated with gender and aging. Journal of cardiovascular development and disease 2019;6(2):19. https://doi.org/10.3390/ jcdd6020019.